AATGAAAGACCCCACCTGTAGGTTTGGCAAGCTAGCTTAAGTAACGCCAT
TTTGCAAGGCATGGAAAAATACATAACTGAGAATAGAAAAGTTCAGATCA
AGGTCAGGAACAGATGGAACAGCTGAATATGGGCCAAAGCGGATATCTGT
GGTAAGCAGTTCCTGCCCCGGCTCAGGGCCAAGAACAGATGGAACAGCTG
AATATGGGCCAAACAGGATATCTGTGGTAAGCAGTTCCTGCCCCGGCTCA
GGGCCAAGAACAGATGGTCCCCAGATGCGGTCCAGCCCTCAGCAGTTTCT
AGAGAACCATCAGATGTTTCCAGGGTGCCCCAAGGACCTGAAATGACCCT
GTGCCTTATTTGAACTAACCAATCAGTTCGCTTCTCGCTTCTGTTCGCGC
GCTTCTGCTCCCCGAGCTCAATAAAAGAGCCCACAACCCCTCACTCGGGG
CGCCAGTCCTCCGATTGACTGAGTCGCCCGGGTACCCGTGTATCCAATAA
ACCCTCTTGCAGTTGCATCCGACTTGTGGTCTCGCTGTTCCTTGGGAGGG
TCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGGTCTTTCATTTGGGGG
CTCGTCCGGGATCGGGAGACCCCTGCCCAGGGACCACCGACCCACCACCG
GGAGGTAAGCTGGCCAGCAACTTATCTGTGTCTGTCCGATTGTCTAGTGT
CTATGACTGATTTTATGCGCCTGCGTCGGTACTAGTTAGCTAACTAGCTC
TGTATCTGGCGGACCCGTGGTGGAACTGACGAGTTCGGAACACCCGGCCG
CAACCCTGGGAGACGTCCCAGGTCGGGGGCCGTTTTTGTGGCCCGACCTG
AGTCCAAAAATCCCGATCGTTTTGGACTCTTTGGTGCACCCCCCTTAGAG
GAGGGATATGTGGTTCTGGTAGGAGACGAGAACCTAAAACAGTTCCCGCC
TCCGTCTGAATTTTTGCTTTCGGTTTGGGACCGAAGCCGCGCCGCGCGTC
TTGTCTGCTGCAGCATCGTTCTGTGTTGTCTCTGTCTGACTGTGTTTCTG
TATTTGTCTGAAAATATGGGCCCGGGCCAGACTGTTACCACTCCCTTAAG
TTTGACCTTAGGTCACTGGAAAGATGTCGAGCGGATCGCTCACAACCAGT
CGGTAGATGTCAAGAAGAGACGTTGGGTTACCTTCTGCTCTGCAGAATGG
CCAACCTTTAACGTCGGATGGCCGCGAGACGGCACCTTTAACCGAGACCT
CATCACCCAGGTTAAGATCAAGGTCTTTTCACCTGGCCCGCATGGACACC
CAGACCAGGTCCCCTACATCGTGACCTGGGAAGCCTTGGCTTTTGACCCC
CCTCCCTGGGTCAAGCCCTTTGTACACCCTAAGCCTCCGCCTCCTCTTCC
TCCATCCGCCCCGTCTCTCCCCCTTGAACCTCCTCGTTCGACCCCGCCTC
GATCCTCCCTTTATCCAGCCCTCACTCCTTCTCTAGGCGCCCCCATATGG
CCATATGAGATCTTATATGGGGCACCCCCGCCCCTTGTAAACTTCCCTGA
CCCTGACATGACAAGAGTTACTAACAGCCCCTCTCTCCAAGCTCACTTAC
AGGCTCTCTACTTAGTCCAGCACGAAGTCTGGAGACCTCTGGCGGCAGCC
TACCAAGAACAACTGGACCGACCGGTGGTACCTCACCCTTACCGAGTCGG
CGACACAGTGTGGGTCCGCCGACACCAGACTAAGAACCTAGAACCTCGCT
GGAAAGGACCTTACACAGTCCTGCTGACCACCCCCACCGCCCTCAAAGTA
GACGGCATCGCAGCTTGGATACACGCCGCCCACGTGAAGGCTGCCGACCC
CGGGGGTGGACCATCCTCTAGACTGCCGGATCCCAGTGTGGTGGTAGGGA
ATTCAAGCTTGATCTCTATAATCTCGCGCAACCTATTTTCCCCTCGAACA
CTTTTTAAGCCGTAGATAAACAGGCTGGGACACTTCACATGAGCGAAAAA
TACATCGTCACCTGGGACATGTTGACAGATCCATGCACGTAAACTCGCAA
GCCGACTGATGCCTTCTGAACAATGGAAAGGCATTATTGCCGTAAGCCGT
GGCGGTCTGGTACCGGTGGGTGAAGACCAGAAACAGCACCTCGATCTGAG
CCGCGATATTGCCCAGCGTTTCAACGCGCTGTATGGCGAGATCGATCCCG
TCGTTTTACAACGTCGTGACTGGGAAAACCCTGGCGTTACCCAACTTAAT
GGCCTTGGAGGACATCCCCCTTTCGCCAGCTGGCGTAATAGCGAAGAGGC

**Figure 1**

CCGCACCGATCGCCCTTCCCAACAGTTGCGCAGCCTGAATTGGCGAATGG
CGCTTTGCCTGGTTTCCGGCACCAGAAGCGGTGCCGGAAAGCTGGCTGGA
GTGCGATCTTCCTGAGGCCGATACTGTCGTCGTCCCCTCAAACTGGCAGA
TGCACGGTTACGATGCGCCCATCTACACCAACGTGACCTATCCCATTACG
GTCAATCCGCCGTTTGTTCCCACGGAGAATCCGACGGGTTGTTACTCGCT
CACATTTAATGTTGATGAAAGCTGGCTACAGGAAGGCCAGACGCGAATT
ATTTTTGATGGCGTTAACTCGGCGTTTCATCTGTGGTGCAACGGGCGCTG
GGTCGGTTACGGCAAGACAGTCGTTTGGCGTCTTAATTTGAGCTCGAGC
GCATATCTACGCGCCGGAGAAAACCGCCTCGCGGTGATGGTGCTGCGCTG
GAGTGACGGGAGTTATCTTGAAGATCAAGATATGTGGCGGATGAGCGGGA
TTCCGAGCGAAAACGGTCTGCGCTGCGGGACGCGCGAATTGAATTATGGC
CCACACCAGAGTGGGCGCGGCGACTTCCAGTTCAACATCAGCCGCTACAG
TCAACAGCAACTGATGGAAACCAGCCATCGCCATCTGCTGCACGCGGAAG
AACCGACATGGCTGTTATACGACGGTTTCCATATGGGGATTGGTGGCGAC
GACTCCTGGAGCCCGTCAGTATCGGCGGAATTCCAGCTGAGCGCCGGTCG
CTACCATTACCAGTTGGTCTGGTGTCAAAAATAATAATAACCGGGCAGGC
CATGTCTGCCCGTATTTCGCGTAAGGAAATCCATTATGTACTATTTAAAC
TCGAGCGGCCGCCAGCACAGTGGTCGACGATAAAATAAAAGATTTTATTT
AGTCTCCAGAAAAAGGGGGGAATGAAAGACCCCACCTGTAGGTTTGGCAA
GCTAGCTTAAGTAACGCCATTTTGGAAGGCATGGAAAAATACATAACTGA
GAATAGAGAAGTTCAGATCAAGGTCAGGAACAGATGGAACAGCTGAATAT
GGGCCAAACAGGATATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGGCC
AAGAACAGATGGAACAGCTGAATATGGGCCAAACAGGATATCTGTGGTAA
GCAGTTCCTGCCCCGGCTCAGGGCCAAGAACAGATGGTCCCCAGATGCGG
TCCAGCCCTCAGCAGTTTCTAGAGAACCATCAGATGTTTCCAGGGTGCCC
CAAGGACCTGAAATGACCCTGTGCCTTATTTGAACTAACCAATCAGTTCG
CTTCTCGCTTCTGTTCGCGCGCTTCTGCTCCCCGAGCTCAATAAAAGAGC
CCACAACCCCTCACTCGGGGCGCCAGTCCTCCGATTGACTGAGTCGCCCG
GGTACCCGTGTATCCAATAAACCCTCTTGCAGTTGCATCCGACTTGTGGT
CTCGCTGTTCCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGTCAGC
GGGGGTCTTTCATTCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGC
GGTTTGCGTATTGGGCGCTCTTCCGCTTCCTCGCTCACTGACTCGCTGCG
CTCGGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAA
TACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCA
AAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTT
TTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAA
GTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCC
CCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGG
ATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCT
CACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGC
TGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAA
CTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAG
CAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACA
GAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATT
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GCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTT

**Figure 1**

TGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTT
GATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAG
GGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTG
CGGCCGGCCGCAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGAC
AGTTACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATT
TCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATAC
GGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCA
CGCTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGC
CGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGTCTATTA
ATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGCGC
AACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCACGCTCGTCGTTTGG
TATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGAT
CCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTT
GTCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACT
GCATAATTCTCTTACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTG
GTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGT
TGCTCTTGCCCGGCGTCAACACGGGATAATACCGCGCCACATAGCAGAAC
TTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACTCTCAA
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AACTGATCTTCAGCATCTTTTACTTTCACCAGCGTTTCTGGGTGAGCAAA
AACAGGAAGGCAAAATGCCGCAAAAAAGGGAATAAGGGCGACACGGAAAT
GTTGAATACTCATACTCTTCCTTTTTCAATATTATTGAAGCATTTATCAG
GGTTATTGTCTCATGAGCGGATACATATTTGAATGTATTTAGAAAAATAA
ACAAATAGGGGTTCCGCGCACATTTCCTGCAT

Figure 1

AATGAAAGACCCCACCTGTAGGTTTGGCAAGCTAGCGCGGCCGCATAACT
TCGTATAGCATACATTATACGAAGTTATTTAATTAAGGCGCGCCTCTAGC
TTAAGTAACGCCATTTTGCAAGGCATGGAAAAATACATAACTGAGAATAG
AGAAGTTCAGATCAAGGTCAGGAACAGATGGAACAGCTGAATATGGGCCA
AACAGGATATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGGCCAAGAAC
AGATGGAACAGCTGAATATGGGCCAAACAGGATATCTGTGGTAAGCAGTT
CCTGCCCCGGCTCAGGGCCAAGAACAGATGGTCCCCAGATGCGGTCCAGC
CCTCAGCAGTTTCTAGAGAACCATCAGATGTTTCCAGGGTGCCCCAAGGA
CCTGAAATGACCCTGTGCCTTATTTGAACTAACCAATCAGTTCGCTTCTC
GCTTCTGTTCGCGCGCTTCTGCTCCCCGAGCTCAATAAAAGAGCCCACAA
CCCCTCACTCGGGGCGCCAGTCCTCCGATTGACTGAGTCGCCCGGGTACC
CGTGTATCCAATAAACCCTCTTGCAGTTGCATCCGACTTGTGGTCTCGCT
GTTCCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGGT
CTTTCATTTGGGGGCTCGTCCGGGATCGGGAGACCCCTGCCCAGGGACCA
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CGATTGTCTAGTGTCTATGACTGATTTTATGCGCCTGCGTCGGTACTAGT
TAGCTAACTAGCTCTGTATCTGGCGGACCCGTGGTGGAACTGACGAGTTC
GGAACACCCGGCCGCAACCCTGGGAGACGTCCCAGGGACTTCGGGGGCCG
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CTGTCTGACTGTGTTTCTGTATTTGTCTGAAAATAAGGGCCCGGGCCAGA
CTGTTACCACTCCCTTAAGTTTGACCTTAGGTCACTGGAAAGATGTCGAG
CGGATCGCTCACAACCAGTCGGTAGATGTCAAGAAGAGACGTTGGGTTAC
CTTCTGCTCTGCAGAATGGCCAACCTTTAACGTCGGATGGCCGCGAGACG
GCACCTTTAACCGAGACCTCATCACCCAGGTTAAGATCAAGGTCTTTTCA
CCTGGCCCGCATGGACACCCAGACCAGGTCCCCTACATCGTGACCTGGGA
AGCCTTGGCTTTTGACCCCCCTCCCTGGGTCAAGCCCTTTGTACACCCTA
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TCTCTCCAAGCTCACTTACAGGCTCTCTACTTAGTCCAGCACGAAGTCTG
GAGACCTCTGGCGGCAGCCTACCAAGAACAACTGGACCGACCGGTGGTAC
CTCACCCTTACCGAGTCGGCGACACAGTGTGGGTCCGCCGACACCAGACT
AAGAACCTAGAACCTCGCTGGAAAGGACCTTACACAGTCCTGCTGACCAC
CCCCACCGCCCTCAAAGTAGACGGCATCGCAGCTTGGATACACGCCGCCC
ACGTGAAGGCTGCCGACCCCGGGGGTGGACCATCCTCTAGACTGCCGGAT
CCCAGTGTGGTGGTAGGGAATTCTTAATTAACGCCACCATGGTGAGCAAG
GGCGAGGAGCTGTTCACCGGGGTGGTGCCCATCCTGGTCGAGCTGGACGG
CGACGTAAACGGCCACAAGTTCAGCGTGTCTGGCGAGGGCGAGGGCGATG
CCACCTACGGCAAGCTGACCCTGAAGTTCATCTGCACCACCGGCAAGCTG
CCCGTGCCCTGGCCCACCCTCGTGACCACCCTGACCTACGGCGTGCAGTG
CTTCAGCCGCTACCCCGACCACATGAAGCAGCACGACTTCTTCAAGTCCG
CCATGCCCGAAGGCTACGTCCAGGAGCGCACCATCTTCTTCAAGGACGAC

**Figure 2**

GGCAACTACAAGACCCGCGCCGAGGTGAAGTTCGAGGGCGACACCCTGGT
GAACCGCATCGAGCTGAAGGGCATCGACTTCAAGGAGGACGGCAACATCC
TGGGGCACAAGCTGGAGTACAACTACAACAGCCACAACGTCTATATCATG
GCCGACAAGCAGAAGAACGGCATCAAGGCGAACTTCAAGATCCGCCACAA
CATCGAGGACGGCAGCGTGCAGCTCGCCGACCACTACCAGCAGAACACCC
CCATCGGCGACGGCCCCGTGCTGCTGCCCGACAACCACTACCTGAGCACC
CAGTCCGCCCTGAGCAAAGACCCCAACGAGAAGCGCGATCACATGGTCCT
GCTGGAGTTCGTGACCGCCGCCGGGATCACTCTCGGCATGGACGAGCTGT
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TACCAGTTGGTCTGGTGTCAAAAATAATAATAACCGGGCAGGCCATGTCT
GCCCGTATTTCGCGTAAGGAAATCCATTATGTACTATTTAAACTCGAGCG
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TATATCGGCATAGTATAATACGACAAGGTGAGGAACTAAACCATGGCCAA
GTTGACCAGTGCCGTTCCGGTGCTCACCGCGCGCGACGTCGCCGGAGCGG
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GTCCAGGACCAGGTGGTGCCGGACAACACCCTGGCCTGGGTGTGGGTGCG
CGGCCTGGACGAGCTGTACGCCGAGTGGTCGGAGGTCGTGTCCACGAACT
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GGCCGAGGAGCAGGACTGAACGCGTCCCGTAGAAAAGATCAAAGGATCTT
CTTGAGATCCTTTTTTTCTGCGCGTAATCTGCTGCTTGCAAACAAAAAAA
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TTTTCCGAAGGTAACTGGCTTCAGCAGAGCGCAGATACCAAATACTGTTC
TTCTAGTGTAGCCGTAGTTAGGCCACCACTTCAAGAACTCTGTAGCACCG
CCTACATACCTCGCTCTGCTAATCCTGTTACCAGTGGCTGCTGCCAGTGG
CGATAAGTCGTGTCTTACCGGGTTGGACTCAAGACGATAGTTACCGGATA
AGGCGCAGCGGTCGGGCTGAACGGGGGGTTCGTGCACACAGCCCAGCTTG
GAGCGAACGACCTACACCGAACTGAGATACCTACAGCGTGAGCTATGAGA
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ATTTTTGTGATGCTCGTCAGGGGGGCGGAGCCTATGGAAAAACGCCAGCA
ACGCGGCCTTTTTACGGTTCCTGGCCTTTTGCTGGCCTTTTGCTCACATA
TCGATTAGTCCAATTTGTTAAAGACAGGATATCAGTGGTCCAGGCTCTAG
TTTTGACTCAACAATATCACCAGCTGAAGCCTATAGAGTACGAGCCATAG
ATAAAATAAAAGATTTTATTTAGTCTCCAGAAAAAGGGGGG

**Figure 2**

```
              •      20       •      40       •      60       •      80
  1 AAGGGCCCGGGCCAGACTGTTACCACTCCCTTAAGTTTGACCTTAGGTCACTGGAAAGATGTCGAGCGGATCGCTCACAA  80
    | |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
  1 ATGGGCCCGGGCCAGACTGTTACCACTCCCTTAAGTTTGACCTTAGGTCACTGGAAAGATGTCGAGCGGATCGCTCACAA  80
              •      20       •      40       •      60       •      80
              •     100       •     120       •     140       •     160
 81 CCAGTCGGTAGATGTCAAGAAGAGACGTTGGGTTACCTTCTGCTCTGCAGAATGGCCAACCTTTAACGTCGGATGGCCGC 160
    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 81 CCAGTCGGTAGATGTCAAGAAGAGACGTTGGGTTACCTTCTGCTCTGCAGAATGGCCAACCTTTAACGTCGGATGGCCGC 160
              •     100       •     120       •     140       •     160
              •     180       •     200       •     220       •     240
161 GAGACGGCACCTTTAACCGAGACCTCATCACCCAGGTTAAGATCAAGGTCTTTTCACCTGGCCCGCATGGACACCCAGAC 240
    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
161 GAGACGGCACCTTTAACCGAGACCTCATCACCCAGGTTAAGATCAAGGTCTTTTCACCTGGCCCGCATGGACACCCAGAC 240
              •     180       •     200       •     220       •     240
              •     260       •     280       •     300       •     320
241 CAGGTCCCCTACATCGTGACCTGGGAAGCCTTGGCTTTTGACCCCCCTCCCTGGGTCAAGCCCTTTGTACACCCTAAGCC 320
    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
241 CAGGTCCCCTACATCGTGACCTGGGAAGCCTTGGCTTTTGACCCCCCTCCCTGGGTCAAGCCCTTTGTACACCCTAAGCC 320
              •     260       •     280       •     300       •     320
              •     340       •     360       •     380       •     400
321 TCCGCCTCCTCTTCCTCCATCCGCCCCGTCTCTCCCCCTTGAACCTCCTCGTTCGACCCCGCCTCGATCCTCCCTTTATC 400
    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
321 TCCGCCTCCTCTTCCTCCATCCGCCCCGTCTCTCCCCCTTGAACCTCCTCGTTCGACCCCGCCTCGATCCTCCCTTTATC 400
              •     340       •     360       •     380       •     400
              •     420       •     440       •     460       •     480
401 CAGCCCTCACTCCTTCTCTAGGCGCCCCCATATGGCCATATGAGATCTTATATGGGGCACCCCCGCCCCTTGTAAACTTC 480
    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
401 CAGCCCTCACTCCTTCTCTAGGCGCCCCCATATGGCCATATGAGATCTTATATGGGGCACCCCCGCCCCTTGTAAACTTC 480
              •     420       •     440       •     460       •     480
              •     500       •     520       •     540       •     560
481 CCTGACCCTGACAAGACAAGAGTTACTAACAGCCCCTCTCTCCAAGCTCACTTACAGGCTCTCTACTTAGTCCAGCACGA 560
    ||||||||||||| ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
481 CCTGACCCTGACATGACAAGAGTTACTAACAGCCCCTCTCTCCAAGCTCACTTACAGGCTCTCTACTTAGTCCAGCACGA 560
              •     500       •     520       •     540       •     560
              •     580       •     600       •     620       •     640
561 AGTCTGGAGACCTCTGGCGGCAGCCTACCAAGAACAACTGGACCGACCGGTGGTACCTCACCCTTACCGAGTCGGCGACA 640
    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
561 AGTCTGGAGACCTCTGGCGGCAGCCTACCAAGAACAACTGGACCGACCGGTGGTACCTCACCCTTACCGAGTCGGCGACA 640
              •     580       •     600       •     620       •     640
              •     660       •     680       •     700       •     720
641 CAGTGTGGGTCCGCCGACACCAGACTAAGAACCTAGAACCTCGCTGGAAAGGACCTTACACAGTCCTGCTGACCACCCCC 720
    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
641 CAGTGTGGGTCCGCCGACACCAGACTAAGAACCTAGAACCTCGCTGGAAAGGACCTTACACAGTCCTGCTGACCACCCCC 720
              •     660       •     680       •     700       •     720
              •     740       •     760       •     780       •     800
721 ACCGCCCTCAAAGTAGACGGCATCGCAGCTTGGATACACGCCGCCCACGTGAAGGCTGCCGACCCCGGGGGTGGACCATC 800
    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
721 ACCGCCCTCAAAGTAGACGGCATCGCAGCTTGGATACACGCCGCCCACGTGAAGGCTGCCGACCCCGGGGGTGGACCATC 800
              •     740       •     760       •     780       •     800
              •     820
801 CTCTAGACTGCCGGATCCCAGTGTGG  (SEQ ID NO:2)                                        826
    ||||||||||||||||||||||||||
801 CTCTAGACTGCCGGATCCCAGTGTGG  (SEQ ID NO:1)                                        826
              •     820

% Identity =   99.8 (824/826)
```

Figure 3

09982223 .101801

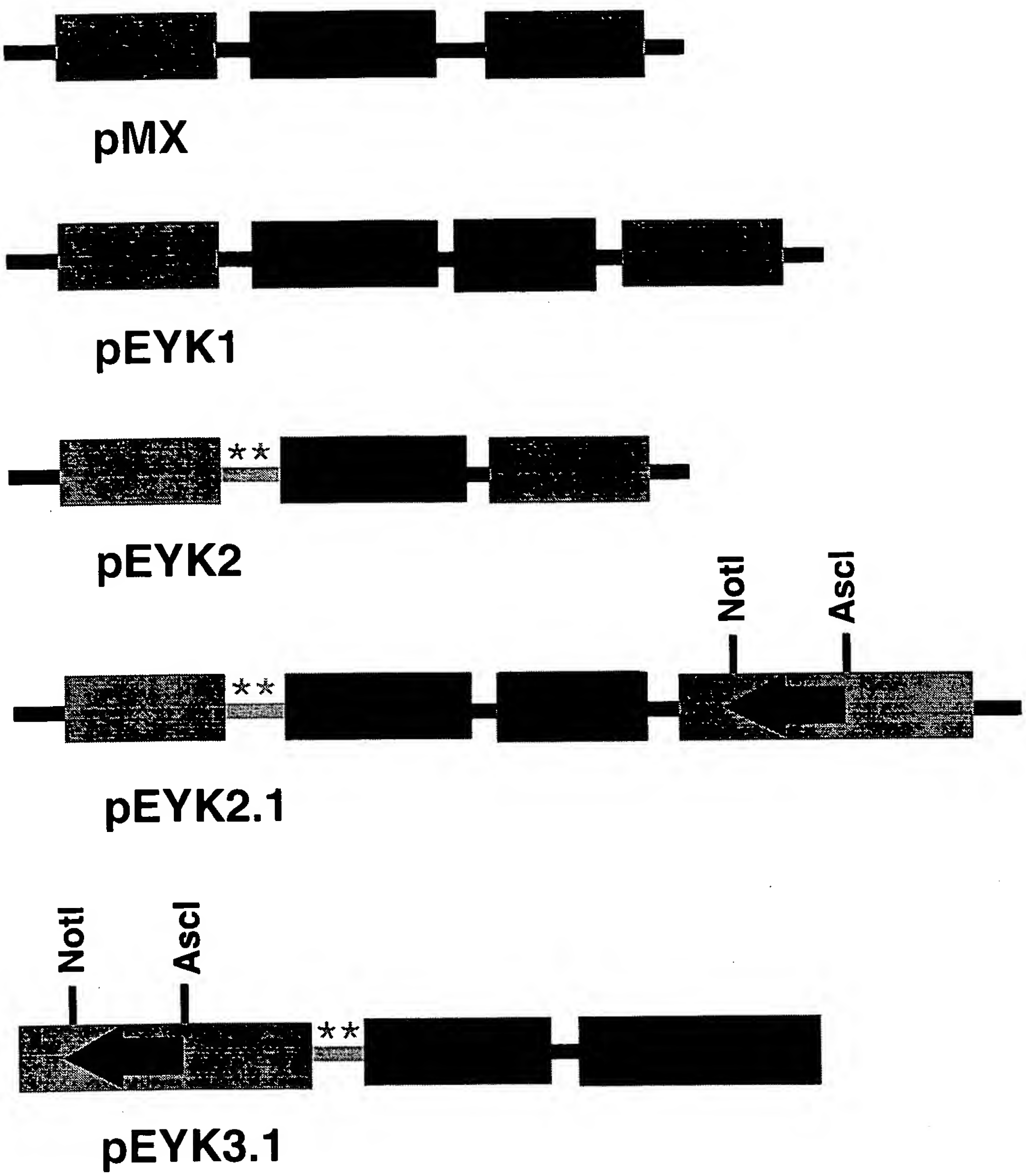


Figure 4

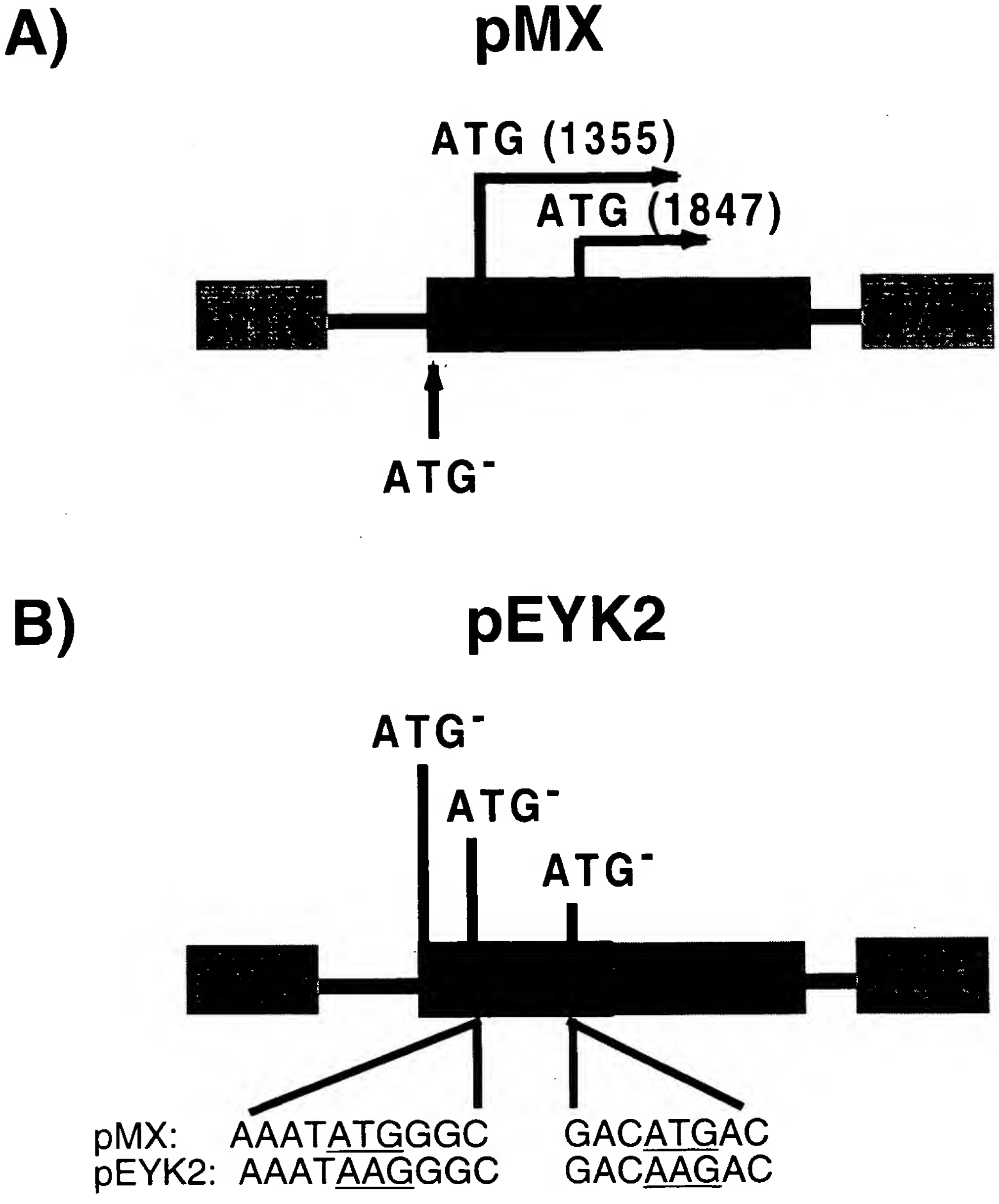

A)
pMX
ATG (1355)
ATG (1847)
ATG⁻
B)
pEYK2
ATG⁻
ATG⁻
ATG⁻
pMX: AAATATGGGC
pEYK2: AAATAAGGGC
GACATGAC
GACAAGAC

Figure 5

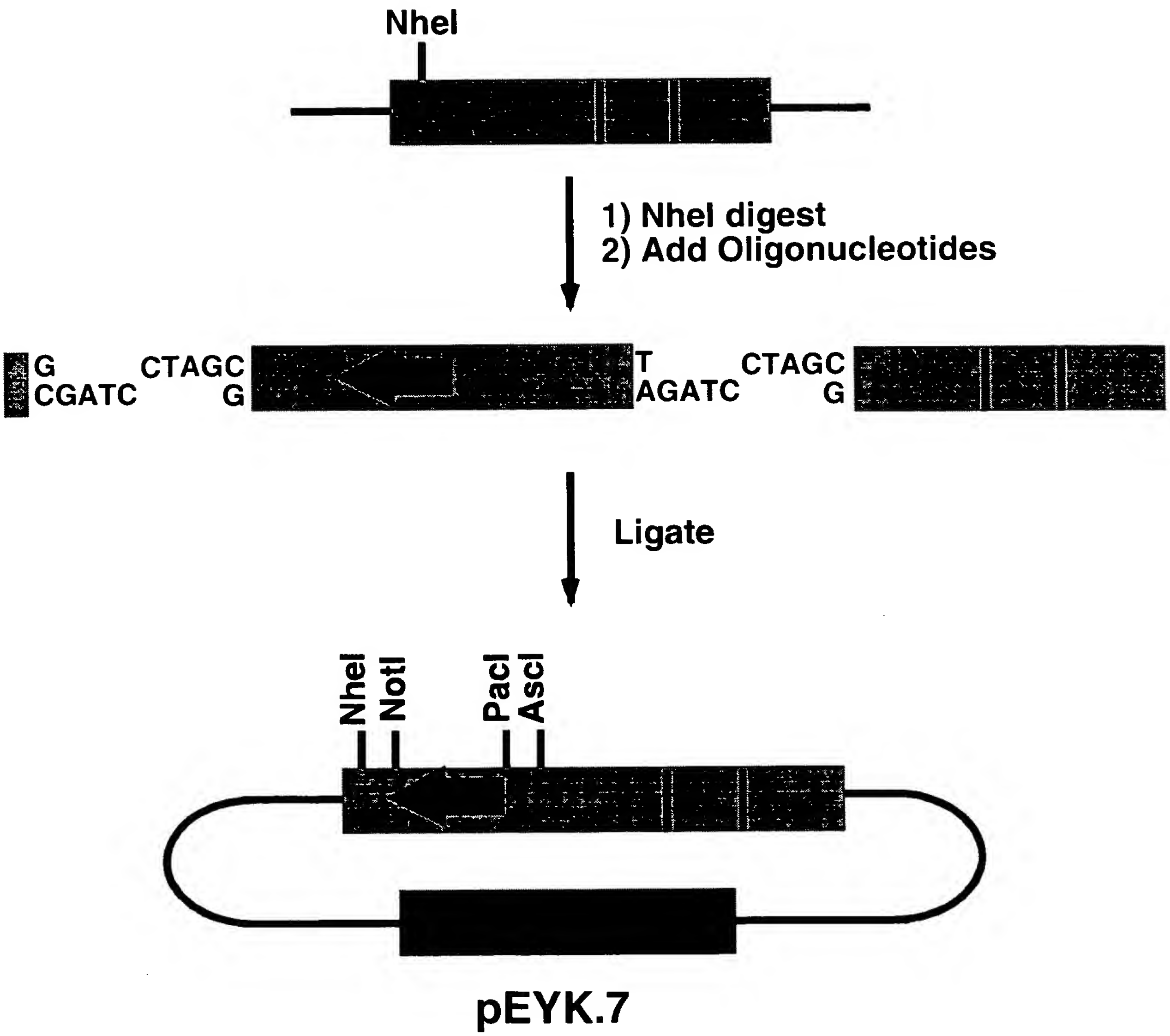

NheI
1) NheI digest
2) Add Oligonucleotides
G
CGATC
CTAGC
G
T
AGATC
CTAGC
G
Ligate
NheI
NotI
PacI
AscI
pEYK.7

Figure 6

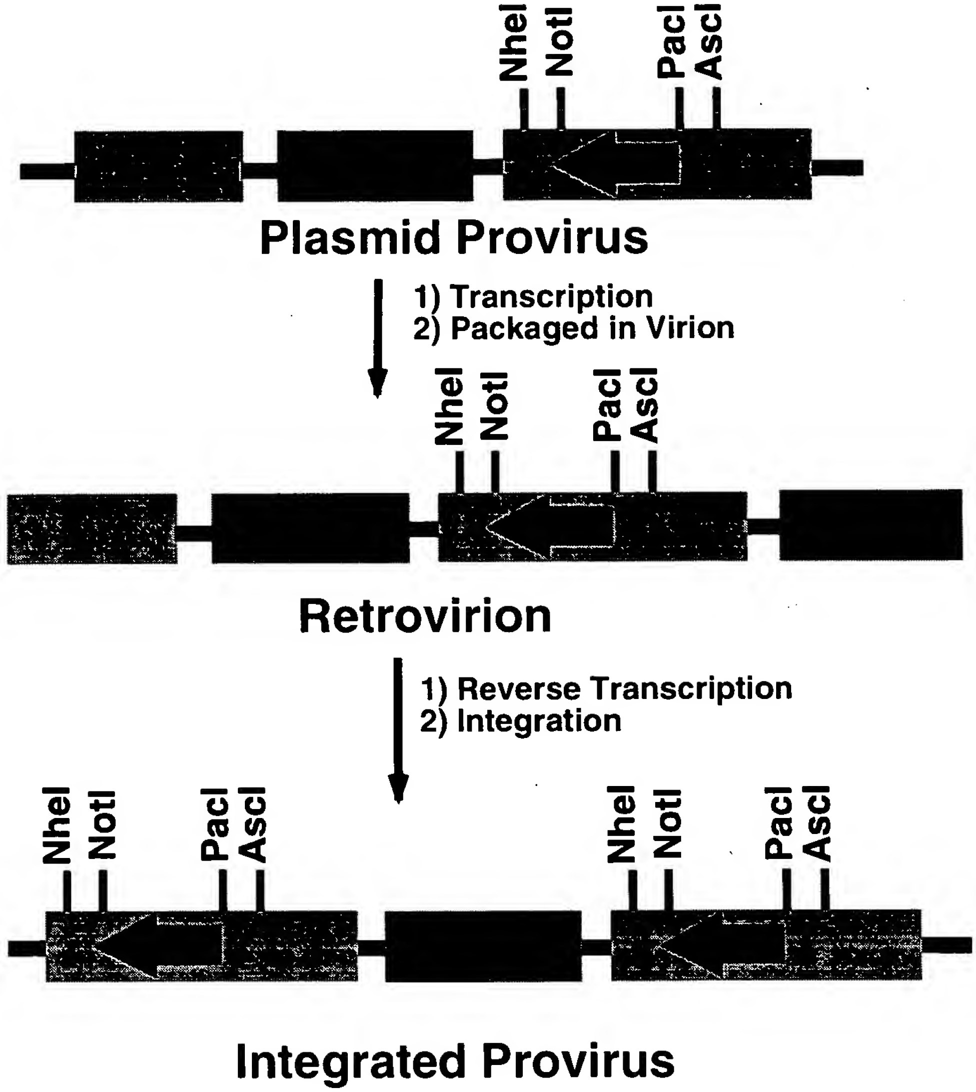

NheI
NotI
PacI
AscI
Plasmid Provirus
1) Transcription
2) Packaged in Virion
NheI
NotI
PacI
AscI
Retrovirion
1) Reverse Transcription
2) Integration
NheI
NotI
PacI
AscI
NheI
NotI
PacI
AscI
Integrated Provirus

Figure 7

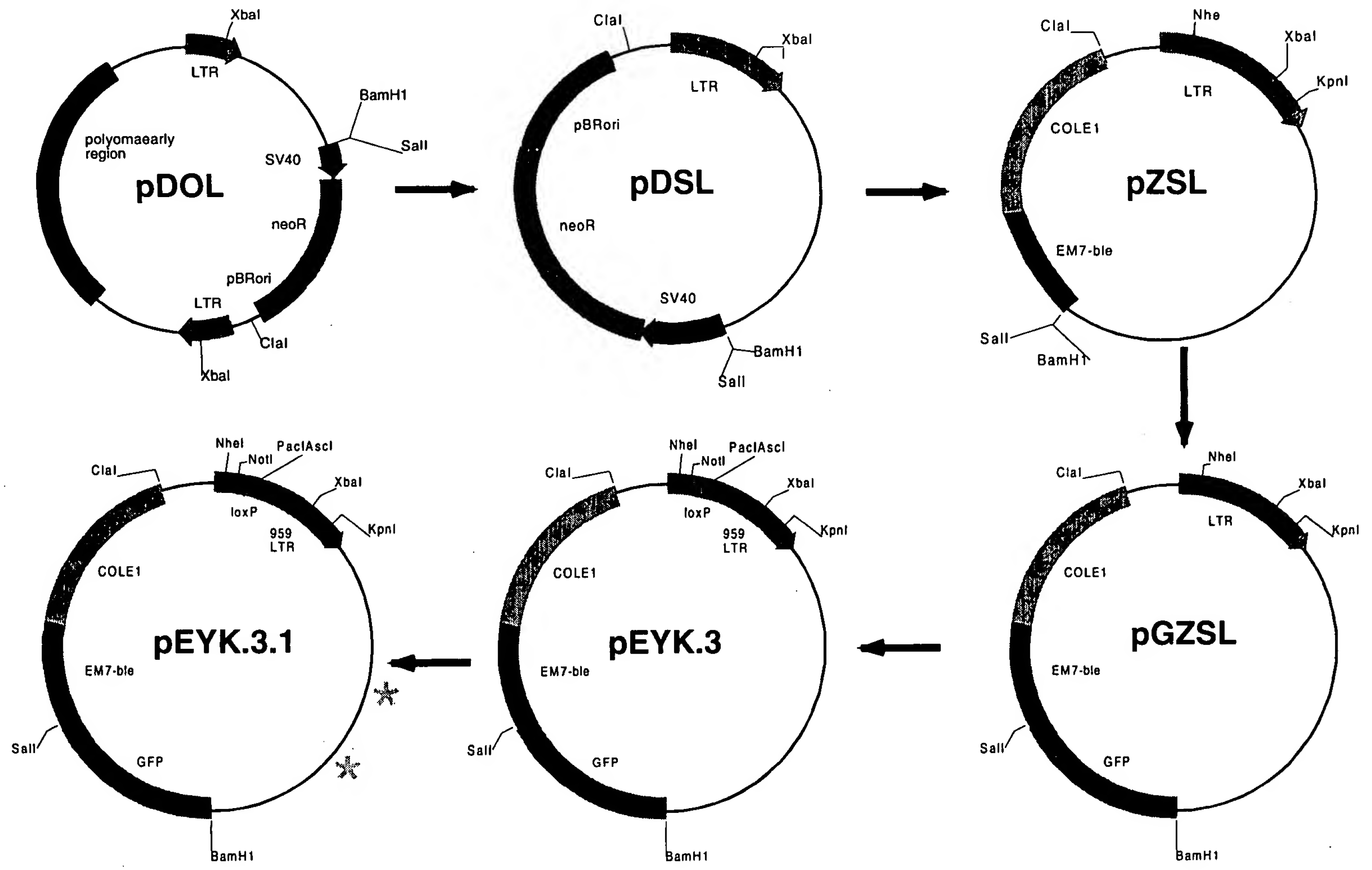
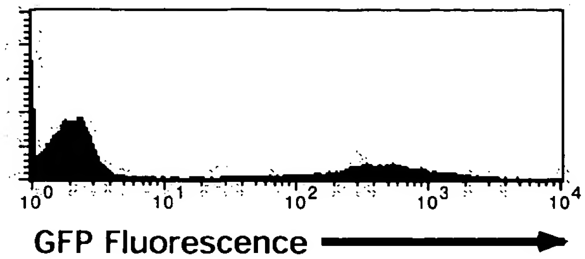

pDOL
Xbal
LTR
BamH1
Sall
polyomaearly region
SV40
neoR
pBRori
LTR
Clal
Xbal
pDSL
Clal
Xbal
LTR
pBRori
neoR
SV40
BamH1
Sall
pZSL
Clal
Nhe
Xbal
Kpnl
LTR
COLE1
EM7-ble
Sall
BamH1
pGZSL
Clal
Nhel
Xbal
Kpnl
LTR
COLE1
EM7-ble
Sall
GFP
BamH1
pEYK.3
Clal
Nhel
Notl
PaclAscl
Xbal
Kpnl
loxP
959 LTR
COLE1
EM7-ble
Sall
GFP
BamH1
pEYK.3.1
Clal
Nhel
Notl
PaclAscl
Xbal
Kpnl
loxP
959 LTR
COLE1
EM7-ble
Sall
GFP
BamH1
*
*

Figure 8

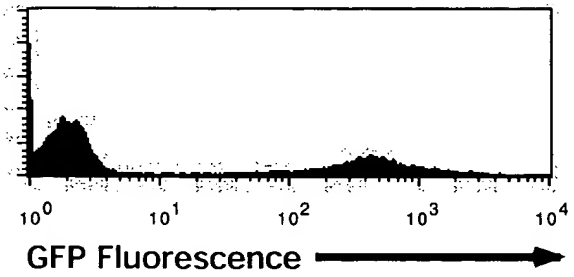
**pEYK.2.2**



Titer: 7.2x$10^6$ IFU / mL

Fold expression: 206

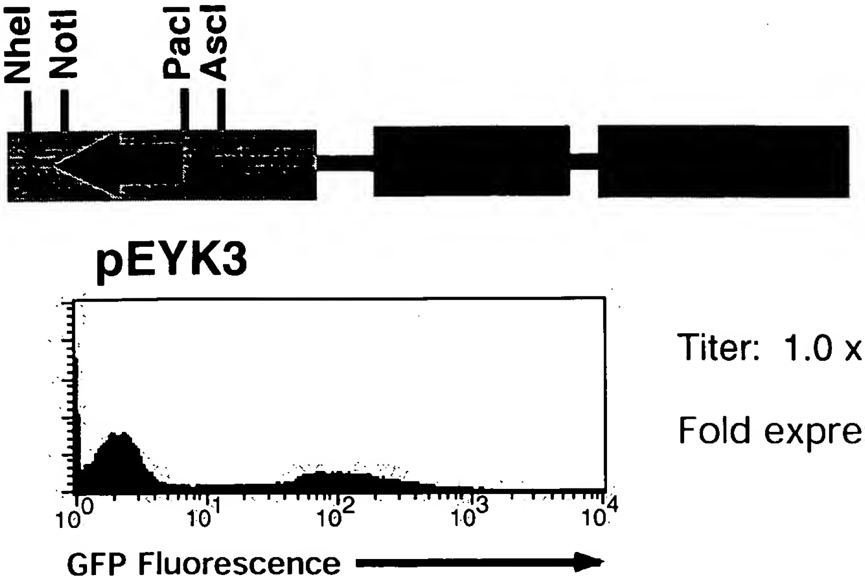
**pEYK.2.3**



Titer: 7.0x$10^6$ IFU / mL

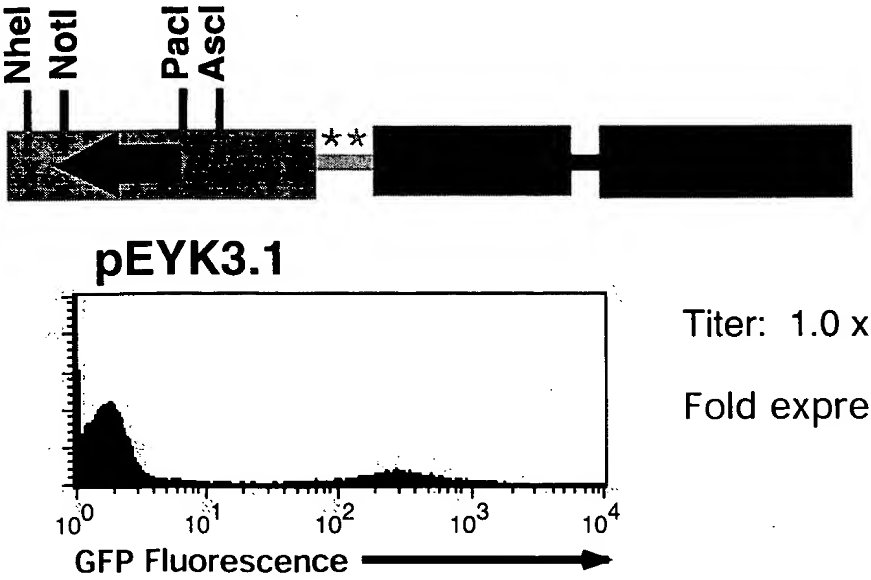
Fold expression: 203

Figure 9



Titer: 1.0 x 10$^6$ IFU / mL

Fold expression: 33



Titer: 1.0 x 10$^6$ IFU / mL

Fold expression: 121

Figure 10

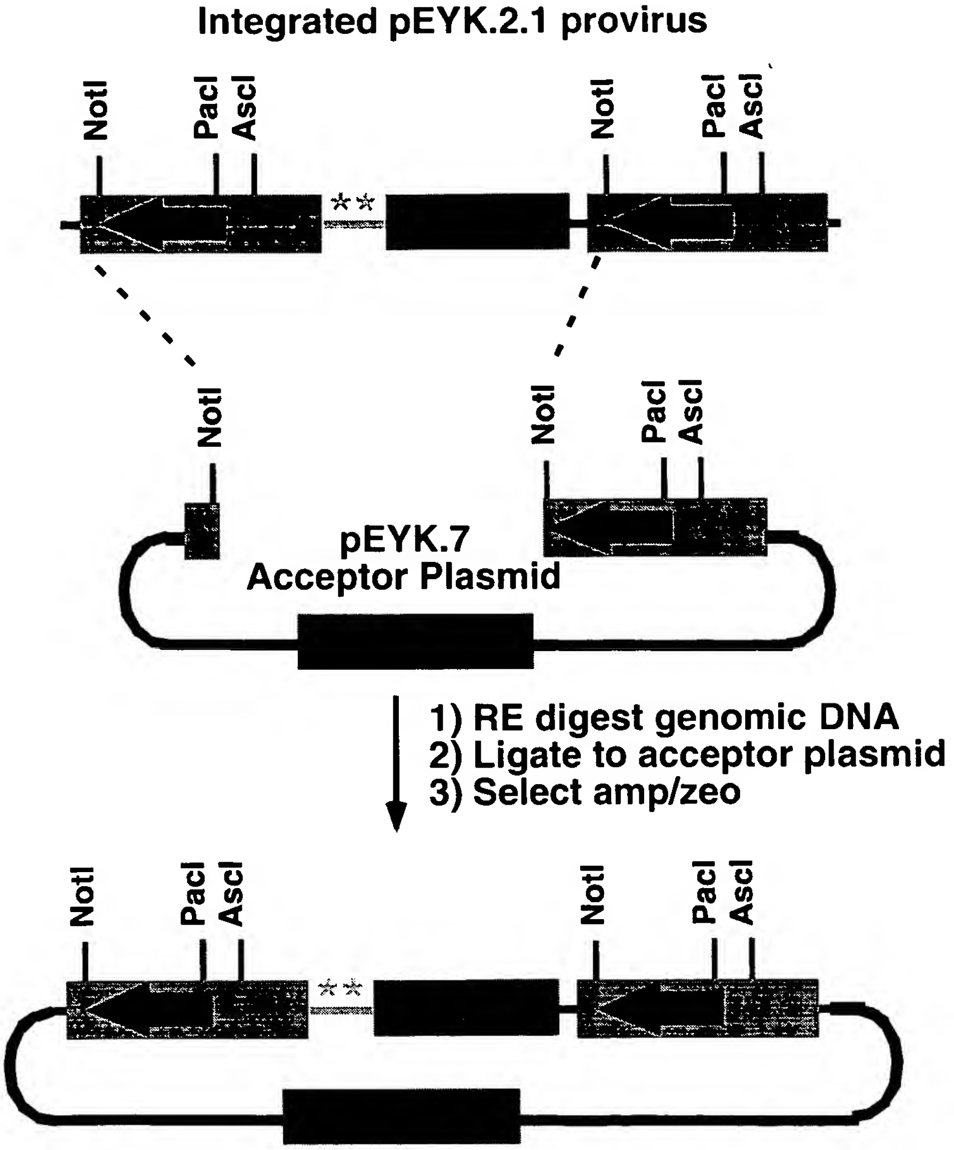

Integrated pEYK.2.1 provirus
NotI
PacI
AscI
NotI
PacI
AscI
**
NotI
NotI
PacI
AscI
pEYK.7
Acceptor Plasmid
1) RE digest genomic DNA
2) Ligate to acceptor plasmid
3) Select amp/zeo
NotI
PacI
AscI
**
NotI
PacI
AscI

Figure 11

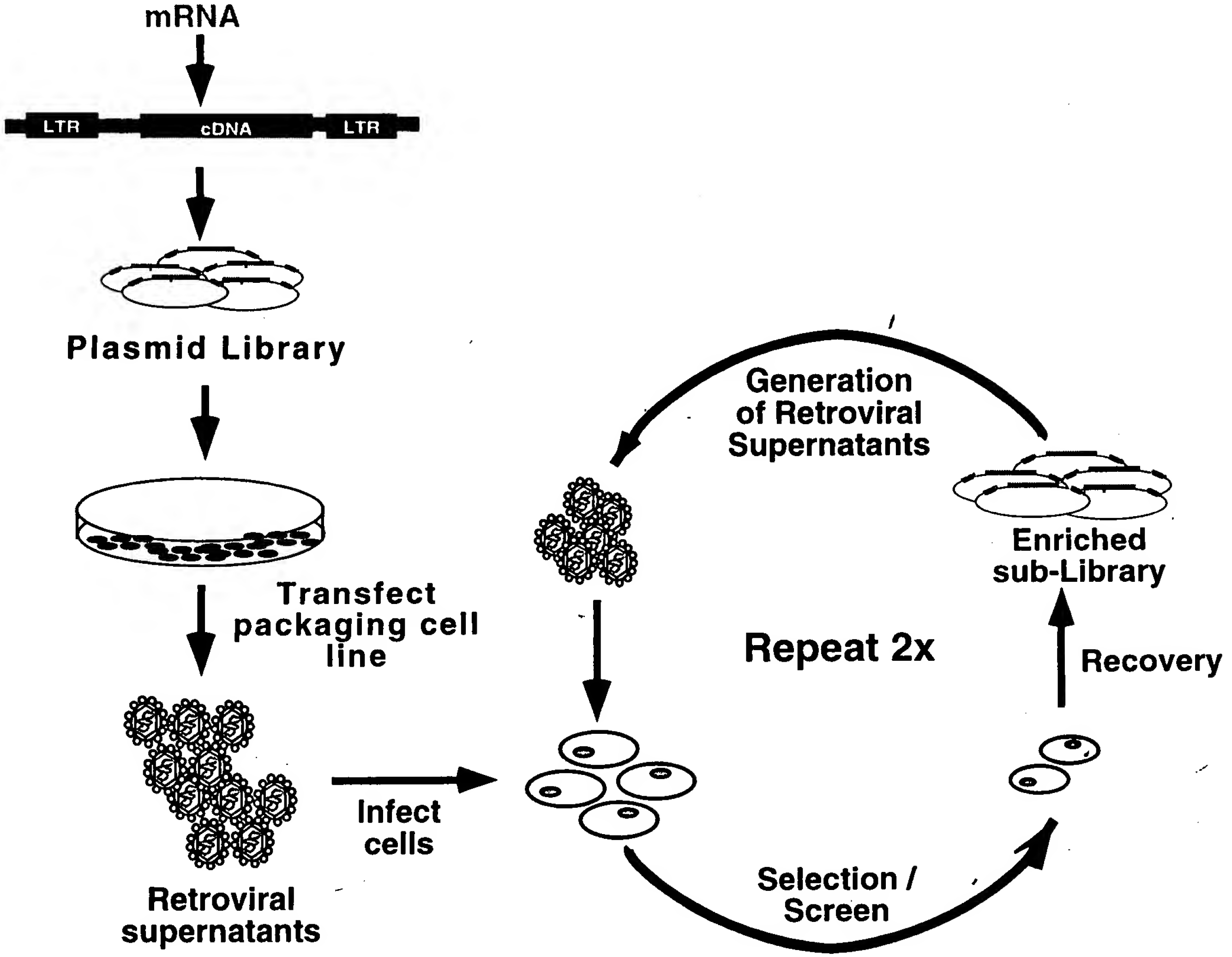

mRNA
LTR
cDNA
LTR
Plasmid Library
Transfect packaging cell line
Retroviral supernatants
Infect cells
Generation of Retroviral Supernatants
Repeat 2x
Enriched sub-Library
Recovery
Selection / Screen

Figure 12

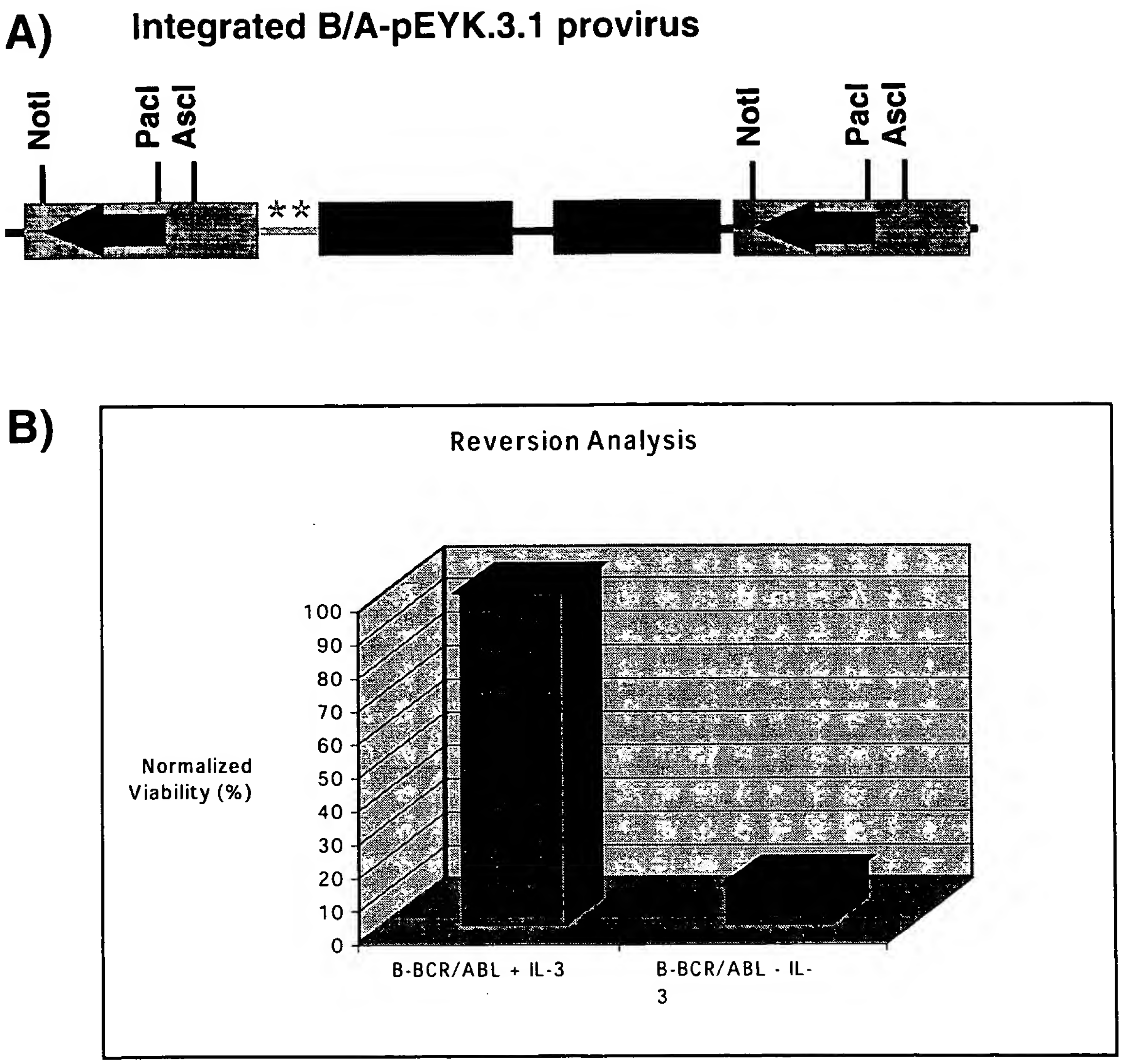

A)
Integrated B/A-pEYK.3.1 provirus
NotI
PacI
AscI
**
NotI
PacI
AscI
B)
Reversion Analysis
Normalized Viability (%)
100
90
80
70
60
50
40
30
20
10
0
B-BCR/ABL + IL-3
B-BCR/ABL - IL-3

Figure 13